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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/052,824 | 11/07/2001 | Fernand Labrie | P/1259-636 | 4181 |
| 2352 | 7590 | 10/02/2007 | EXAMINER | |
| OSTROLENK FABER GERB & SOFFEN 1180 AVENUE OF THE AMERICAS NEW YORK, NY 100368403 | | | | CHONG, YONG SOO |
| ART UNIT | | PAPER NUMBER | | |
| 1617 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 10/02/2007 | | | | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | |
|------------------------------|---------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 10/052,824 | LABRIE, FERNAND |
| | Examiner Yong S. Chong | Art Unit 1617 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 07 August 2007.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-3 and 14-28 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-3 and 14-28 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date 8/7/07.

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____.
 5) Notice of Informal Patent Application
 6) Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/7/2007 has been entered.

Claim(s) 4-13 have been cancelled. Claim(s) 1-3, 14-28 are pending. Claim(s) 1-2, 14, 26 have been amended. Claim(s) 1-3, 14-28 are examined herein.

Applicant's amendments have rendered the 112 and the double patenting rejections of the last Office Action moot, therefore hereby withdrawn.

Applicant's arguments have been fully considered but found not persuasive. The 103(a) rejection of the last Office Action is maintained for reasons of record and modified below as a result of the new claim amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, and 14-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Labrie (5,362,720), and Labrie et al. (WO 96/26201), and Applicant's admission regarding the prior art in the specification at 2 lines 3-4, for the same reasons of record in the previous Office Action November 18, 2004.

Labrie (5,362,720) teaches that estrogens such as 17 β -estradiol are well known to be used in estrogen therapy in menopausal women. However, estrogens are known to induce estrogen-dependent diseases such as breast cancer. Labrie also discloses that androgenic compounds or androgenic steroids are useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer. See abstract, col.1 line 35-38, col.4 lines 45-48, col.10, and claims 1-30.

Labrie et al. (WO 96/26201) discloses that the particular SERM, EM-652 (the instant elected species) or its pharmaceutically acceptable salts such as EM-652.HCl, have anti-estrogen activities and are therefore useful in methods of treating estrogen sensitive or estrogen-dependent diseases such as breast cancer, which is known estrogen-induced effects. See abstract, page 1, page 6-8, 10, and 19-21, and claims 11-12.

Applicant's admission regarding the prior art in the specification at 2 lines 3-4 teaches that Hormone Replace Therapy (e.g., administration of estrogens) is known to be useful in treatment of menopausal symptoms.

The prior art does not expressly disclose the employment of the combination of an estrogen such as 17β -estradiol and the particular SERM, EM-652.HCl, or maybe further combining an androgenic compound in a method of reducing or eliminating the incidence of menopausal symptoms.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as 17β -estradiol and the particular SERM, EM-652.HCl, or to further combine an androgenic compound in a method of reducing or eliminating the incidence of menopausal symptoms.

One having ordinary skill in the ad at the time the invention was made would have been motivated to employ the combination of an estrogen such as 17β -estradiol and the particular SERM, EM-652.HCl, or to further combine an androgenic compound in a method of reducing or eliminating the incidence of menopausal symptoms, since estrogens such as 17β -estradiol is well known in the art to be used in estrogen therapy or Hormone Replace Therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms.

Moreover, 17β -estradiol in combination with androgenic compounds or androgenic steroids is known to be capable to inhibiting breast tumor or cancer growth, and are therefore useful in methods of treating estrogen-dependent diseases, e.g., breast cancer according to Labrie. Fudher, the particular SERM, EM-652.HCl, is known

to be in methods of treating estrogen-dependent diseases. Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as $\text{I}7\beta\text{-estradiol}$ and the particular SERM, EM-652.HCl, or further combining an androgenic compound would be useful in reducing or eliminating the incidence of menopausal symptoms, while reducing the risk of or treating estrogen-dependent diseases such as breast cancer induced by estrogens during estrogen therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms, since each of components herein is known to be useful in the same treatment, i.e., treating estrogen-dependent diseases.

Since all active composition components herein are known to be useful to reduce or treat estrogen-dependent diseases, it is considered *prima facie* obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected.

See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly *prima facie* obvious over the teachings of the prior art.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Labrie (5,362,720), and Labrie (5,780,460, PTO-892), and Labrie et al. (WO 96/26201), and Applicant's admission regarding the prior art in the specification at 2 lines 3-4 for the same reasons of record in the previous Office Action dated November 18, 2004.

Labrie (5,36),720 teaches that estrogens such as $\text{I}7\beta\text{-estradiol}$ are well known to be used in estrogen therapy in menopausal women. However, estrogens are known

to induce estrogen-dependent diseases such as breast cancer. Labrie also discloses that androgenic compounds or androgenic steroids are useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer. See abstract, col.1 line 35-38, col.4 lines 45-48, col.10, and claims 1-30.

Labrie (5,780,460) discloses that sex steroid precursors such as DEHA alone or in combination with an estrogen are useful in method of reducing or eliminating the incidence of menopausal symptoms, e.g., vaginal atrophy and diminished libido, and also useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer. See abstract, col. 1-2, col.3 lines 44-55, and claims 1-2.

Labrie et al. (WO 96/26201) discloses that the particular SERM, EM-652 (the instant elected species) or its pharmaceutically acceptable salts such as EM-652.HCl, have anti-estrogen activities and are therefore useful in methods of treating estrogen sensitive or estrogen-dependent diseases such as breast cancer, which is known estrogen-induced effects. See abstract, page 1, page 6-8, 10, and 19-21, and claims 11-12.

Applicant's admission regarding the prior ad in the specification at pg. 2 lines 3-4 teaches that Hormone Replace Therapy (e.g., administration of estrogens) is known to be useful in treatment of menopausal symptoms.

The prior art does not expressly disclose the employment of the combination of an estrogen such as 17 β -estradiol and the particular SERM, EM-652.HCl, and DHEA in a method of reducing or eliminating the incidence of menopausal symptoms.

It would have been obvious to a person of ordinary skill in the art at the time the

invention was made to employ of the combination of an estrogen such as $\text{I}7\beta\text{-estradiol}$ and the particular SERM, EM-652.HCl, and DHEA in a method of reducing or eliminating the incidence of menopausal symptoms.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as $\text{I}7\beta\text{-estradiol}$ and the particular SERM, EM-652.HCl, and DHEA in a method of reducing or eliminating the incidence of menopausal symptoms, since estrogens such as $\text{I}7\beta\text{-estradiol}$ are well known in the art to be used in estrogen therapy or Hormone Replace Therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms. Moreover, sex steroid precursors such as DEHA alone or in combination with an estrogen (e.g., $\text{I}7\beta\text{-estradiol}$) is known to be useful in method of reducing or eliminating the incidence of menopausal symptoms, and also useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer according to Labrie. Androgenic compounds are also known to be useful in methods of treating estrogen-dependent diseases. Further, the particular SERM, EM-652.HCl, is known to be in methods of treating estrogen-dependent diseases.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as $\text{I}7\beta\text{-estradiol}$ and the particular SERM, EM-652.HCl, and DHEA, or further combining an androgenic compound would be useful in reducing or eliminating the incidence of menopausal symptoms, while reducing the risk of or treating estrogen-dependent diseases such as breast cancer induced by estrogens during estrogen therapy in menopausal women for reducing or eliminating the incidence

of menopausal symptoms, since each of components herein is known to be useful in the same treatment, i.e., treating estrogen-dependent diseases.

Since all active composition components herein are known to be useful to reduce or treat estrogen-dependent diseases, it is considered *prima facie* obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected.

See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly *prima facie* obvious over the teachings of the prior art.

Response to Arguments

Applicant argues against the cited prior art references because the term "estrogen-dependent diseases" fails to distinguish between menopause (a condition discussed in one of the cited references), which responds favorably to estrogens, while breast cancer (from another reference) is known to respond favorably. Applicant also argues that it is improper to combine two pharmaceuticals whose mechanisms of action are known to be in conflict. For example, estrogens are known to activate the estrogen receptor, while anti-estrogens are known to block the access of estrogens to the estrogen receptor, thus diminishing the activation of the estrogen receptor.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on

the combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Furthermore, there does not need to be a distinction between menopause and breast cancer because as stated in the rejection, estrogen therapy in menopausal women may induce estrogen-dependent diseases such as breast cancer. Therefore, in this manner, menopause and breast cancer are linked.

Applicant's arguments with respect to the biological mechanism of action are not persuasive because it is merely an inherent property of the composition being administered to the same patient population. Furthermore, Applicant is essentially arguing against the instant invention since no argument has been made against the active agents, dosage, or patient population.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Yong S. Chong